Primary results of the phase III JAVELIN head & neck 100 trial: Avelumab plus chemoradiotherapy (CRT) followed by avelumab maintenance vs CRT in patients with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)


Medical Oncology, Moores Cancer Center, University of California, La Jolla, CA, USA, 2 Medical Oncology, UPMC Hillman Cancer Center, Pittsburgh, PA, USA, 3 Internal Medicine/Medical Oncology, Attikon University Hospital, Athens, Greece, 4 Division of Head and Neck Oncology, Dana Farber Cancer Institute, Boston, MA, USA, 5 Head and Neck Medical Oncology Dept., National Cancer Center Hospital East, Kashiwa, Japan, 6 Radiation Oncology, CHUV - Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, 7 Dept. of Radiotherapy and Imaging, ICR - Institute of Cancer Research - Chester Beatty Laboratories, London, UK, 8 Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, 9 Department of Radiation Oncology, Changhua Christian Hospital, Changhua, Taiwan, 10 Internal Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA, 11 Medical Oncology, Instituto Português Oncologia de Coimbra Francisco Gentil E. P. E. (IPO Coimbra), Coimbra, Portugal, 12 Department of Radiation Oncology, National Institute of Oncology Hungary, Budapest, Hungary, 13 Radiation Oncology, CHP Saint-Grégoire, St. Grégoire, France, 14 Medical Oncology, Hospital Costa del Sol, Marbella, Spain, 15 Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, 16 Clinical Oncology Dispensary, Budgetary Institution of Healthcare of the Omsk Region, Omsk, Russian Federation, 17 Global Product Development, Pfizer AG / Pfizer PFE Switzerland GmbH, Zurich, Switzerland, 18 Biostatistics, Pfizer Inc., La Jolla, CA, USA, 19 Oncology, Pfizer Inc - USA, San Diego, CA, USA 20 Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background
Despite high-dose, cisplatin-containing, multimodality therapy, LA SCCHN ultimately recurs in many patients. This trial investigated whether avelumab, a human anti–PD-L1 antibody, improved progression-free survival (PFS) when combined with concurrent CRT followed by avelumab maintenance.

Methods
This randomized, double-blind, placebo-controlled phase III trial (JAVELIN Head and Neck 100; NCT02952586) included patients with histologically confirmed, previously untreated LA SCCHN of the oropharynx, hypopharynx, larynx, or oral cavity eligible for definitive CRT with curative intent. Patients were required to have stage III, IVa, or IVb disease per AJCC (7th edition) except for HPV+ oropharyngeal patients, for whom only T4 or N2c or N3 status was allowed. Patients were randomized 1:1 to receive avelumab 10 mg/kg IV Q2W + CRT (cisplatin 100 mg/m² Q3W + standard fractionation of 70 Gy in 35 fractions over 7 weeks) or placebo + CRT. This was preceded by a lead-in dose and followed by avelumab or placebo maintenance therapy for up to 1 year. The primary endpoint was PFS by investigator assessment per modified RECIST v1.1; interim analysis was planned at 217 events.

Results
697 patients were randomized (avelumab arm, n=350; placebo arm, n=347); baseline characteristics were similar in both arms. At interim analysis, the hazard ratios for PFS per modified RECIST v1.1 (based on 224 events) and overall survival (OS; based on 131 deaths) were 1.21 (95% CI: 0.93-1.57; p=0.920) and 1.31 (95% CI: 0.93-1.85; p=0.937), respectively, both in favor of placebo + CRT. Median PFS and OS were not reached in either arm. Grade ≥3 adverse events (AEs) were more frequent with avelumab + CRT vs placebo + CRT (88% vs 82%); fatal AEs occurred in 6% and 5%, respectively. Rates of AEs leading to discontinuation of any study drug were similar in both arms (33% vs 32% in the avelumab vs placebo arms).

Conclusions
Tolerability was similar in both arms; however, the study did not demonstrate statistically significant improvement in PFS with avelumab + CRT vs placebo + CRT. These results may inform future trial design.

Clinical trial identification
NCT02952586.
Medical writing assistance was provided by Eleanor Green of ClinicalThinking and funded by Pfizer and Merck KGaA, Darmstadt, Germany.

**Legal entity responsible for the study**

Merck KGaA, Darmstadt, Germany and Pfizer.

**Funding**

Pfizer, as part of an alliance between Merck KGaA, Darmstadt, Germany, and Pfizer.

**Disclosure**

E.E. Cohen: Advisory/Consultancy: Amgen; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Bayer; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Incyte; Advisory/Consultancy: Merck Sharp & Dohme; Advisory/Consultancy: Merck KGaA, Darmstadt, Germany. R.L. Ferris: Advisory/Consultancy: Aduro Biotech, Inc; Advisory/Consultancy: Amgen; Advisory/Consultancy, Research grant/Funding (institution): AstraZeneca/MedImmune; Advisory/Consultancy: Bain Capital Life Sciences; Advisory/Consultancy, Research grant/Funding (institution): Bristol-Myers Squibb; Advisory/Consultancy: EMD Serono; Advisory/Consultancy: GlaxoSmithKline; Advisory/Consultancy: Iovance Biotherapeutics, Inc; Advisory/Consultancy: Lilly; Advisory/Consultancy: MacroGenics, Inc.; Advisory/Consultancy, Research grant/Funding (institution): Merck; Advisory/Consultancy: Nanobiotix; Advisory/Consultancy: Numab Therapeutics AG; Advisory/Consultancy: Oncorus, Inc.; Advisory/Consultancy: Ono Pharmaceutical Co. Ltd; Advisory/Consultancy: Pfizer; Advisory/Consultancy: PPD; Advisory/Consultancy: Regeneron Pharmaceuticals; Advisory/Consultancy, Research grant/Funding (institution): Tesaro; Advisory/Consultancy: Torque Therapeutics Inc; Advisory/Consultancy, Research grant/Funding (institution): TTMS; Research grant/Funding (institution): VentiRx Pharmaceuticals. A. Psyrri: Honoraria (self), Advisory/Consultancy, Research grant/Funding (self): BMS; Honoraria (self), Advisory/Consultancy, Research grant/Funding (self): MSD; Honoraria (self), Research grant/Funding (self), Travel/Accommodation/Expenses: Roche; Honoraria (self), Advisory/Consultancy: Merck Serono; Honoraria (self), Advisory/Consultancy: Pfizer; Advisory/Consultancy, Research grant/Funding (self): KURA; Research grant/Funding (self): Genesis; Research grant/Funding (self): DEMO; Travel/Accommodation/Expenses: Ipsen. R. Haddad: Advisory/Consultancy, Research grant/Funding (self): Merck; Advisory/Consultancy, Research grant/Funding (self): BMS; Advisory/Consultancy, Research grant/Funding (self): Pfizer; Advisory/Consultancy, Research grant/Funding (self): Genentech; Advisory/Consultancy, Research grant/Funding (self): TTMS; Research grant/Funding (self): GSK; Advisory/Consultancy, Research grant/Funding (self): AstraZeneca. M. Tahara: Honoraria (self): Eisai; Honoraria (self): Merck Serono; Honoraria (self), Advisory/Consultancy, Research grant/Funding (self): AstraZeneca; Advisory/Consultancy, Research grant/Funding (self): MSD; Advisory/Consultancy, Research grant/Funding (self): Bayer; Advisory/Consultancy, Research grant/Funding (self): Pfizer; Advisory/Consultancy, Research grant/Funding (self): AstraZeneca; Advisory/Consultancy, Research grant/Funding (self): Celgene; Advisory/Consultancy: Amgen; Research grant/Funding (self): Novartis. K.J. Harrington: Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): AstraZeneca; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: BMS; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: MSD; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Merck-Serono; Honoraria (institution), Advisory/Consultancy: Pfizer; Honoraria (institution), Advisory/Consultancy, Speaker Bureau/Expert testimony: Regimmune; Advisory/Consultancy, Research grant/Funding (institution): Bl. J.-C. Lin: Travel/Accommodation/Expenses: Taiwan Merck; Travel/Accommodation/Expenses: ONO; Travel/Accommodation/Expenses: MSD. M. Razaq: Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Merck; Advisory/Consultancy: Aspyrian; Speaker Bureau/Expert testimony, Shareholder/Stockholder/Stock options: Merck & co; Shareholder/Stockholder/Stock options: AbbVie. J. Lovey: Honoraria (self): Nutricia; Honoraria (self): Merck. J. Chamois: Travel/Accommodation/Expenses: Amgen; Travel/Accommodation/Expenses: Astellas; Travel/Accommodation/Expenses: MSD. A. Rueda Dominguez: Advisory/Consultancy, Speaker Bureau/Expert testimony: Merck; Advisory/Consultancy, Speaker Bureau/Expert testimony: BMS; Advisory/Consultancy, Speaker Bureau/Expert testimony: Roche; Speaker Bureau/Expert testimony: Takeda. S. De Beukelaer, H. Thurm: Full/Part-time employment: Pfizer. D. Pavlov: Shareholder/Stockholder/Stock options, Full/Part-time employment: Pfizer. N. Lee: Advisory/Consultancy, Research grant/Funding (self); Pfizer; Advisory/Consultancy, Research grant/Funding (self): Merck; Advisory/Consultancy: Merck Serono; Advisory/Consultancy: Lilly; Research grant/Funding (self): AstraZeneca. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology